

WHAT IS CLAIMED IS:

1. A method for diagnosis of an inflammatory, a fibrotic or a cancerous disease in a patient comprising the steps of:
 - 5 a) measuring the values of biochemical markers in the serum or plasma of said patient,
 - b) combining said values through a logistic function including said markers and,
 - c) analyzing the end value of said logistic function in order to
 - 10 determine the presence of liver fibrosis and/or liver necroinflammatory lesions in said patient.
2. The method of claim 1, wherein said disease is liver fibrosis and/or presence of liver necroinflammatory lesions.
3. The method of claim 1, wherein the logistic function is obtained through the
 - 15 following method:
 - i) classification of the patients in different groups according to the extend of their disease;
 - ii) identification of factors which differ significantly between these groups by unidimensional analysis;
 - 20 iii) logistic regression analysis to assess the independent discriminative value of markers for the diagnosis of fibrosis and/or liver necroinflammatory lesions
 - iv) construction of the logistic function by combination of these identified independent factors.
- 25 4. The method of claim 1, wherein at least 4 biochemical markers are studied in step a).
5. The method of claim 1, wherein said markers are chosen in the group consisting of α 2-macroglobulin, AST, ALT, GGT, γ -globulin, total bilirubin, albumin, α 1-globulin, α 2-globulin, haptoglobin, β -globulin, apoA1, IL10, TGF- β 1, apoA2,
 - 30 apoB.
6. The method of claim 1, wherein the logistic function further takes the age and gender of the patient into account.

7. The method of claim 2, wherein said measured biochemical markers used for diagnosis of fibrosis include α 2-macroglobulin, GGT, γ -globulin, total bilirubin, (α 2-globulin or haptoglobin) and apoA1.
8. The method of claim 2, wherein said measured biochemical markers used for diagnosis of presence of necroinflammatory lesions include α 2-macroglobulin, GGT, γ -globulin, (ALT or AST) and apoA1.
9. The method of claim 2, wherein the logistic function is chosen in the group consisting of:

$$- f1 = a_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - a_2 \times [\alpha 2\text{-globulin (g/l)}] + a_3 \times \text{Log} [\text{GGT (IU/l)}] + a_4 \times [\gamma\text{-globulin (g/l)}] + a_5 \times [\text{Age (years)}] + a_6 \times \text{Log} [\text{Bilirubin (umol/l)}] - a_7 \times [\text{ApoA1 (g/l)}] + a_8 \times [\text{Sex (female=0, male=1)}] - a_9, \text{ with}$$

- a_1 comprised between 6.5 and 6.9,
- a_2 comprised between 0.450 and 0.485,
- a_3 comprised between 1.100 and 1.300,
- a_4 comprised between 0.0700 and 0.0750,
- a_5 comprised between 0.0265 and 0.0300,
- a_6 comprised between 1.400 and 1.700,
- a_7 comprised between 0.900 and 1,
- a_8 comprised between 0.300 and 0.450, and
- a_9 comprised between 4.200 and 4.700.

$$- f2 = b_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - b_2 \times [\alpha 2\text{-globulin (g/l)}] + b_3 \times \text{Log} [\text{GGT (IU/l)}] + b_4 \times [\gamma\text{-globulin (g/l)}] + b_5 \times [\text{Age (years)}] + b_6 \times \text{Log} [\text{Bilirubin (umol/l)}] - b_7 \times [\text{ApoA1 (g/l)}] + b_8 \times [\text{Sex (female=0, male=1)}] + b_9 [\text{Albumin (g/l)}] + b_{10} [\alpha 1\text{-globulin (g/l)}] - b_{11} [\beta 2\text{-globulin (g/l)}] 2.189 - b_{12} \times \text{Log} [\text{ALT (IU/l)}] - b_{13}, \text{ with}$$

- b_1 comprised between 9.9 and 10.2,
- b_2 comprised between 0.7 and 0.77,
- b_3 comprised between 2 and 2.4,
- b_4 comprised between 0.1 and 0.2,
- b_5 comprised between 0.04 and 0.07,
- b_6 comprised between 4 and 4.6,

- b_7 comprised between 2 and 2.5,
- b_8 comprised between 0.28 and 0.32
- b_9 comprised between 0.025 and 0.04
- b_{10} comprised between 2 and 2.2
- b_{11} comprised between 0.1 and 0.16
- b_{12} comprised between 0.7 and 0.9, and
- b_{13} comprised between 12 and 14.

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- $f3 = c_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - c_2 \times [\beta 2\text{-globulin (g/l)}] + c_3 \times \text{Log} [\text{GGT (IU/l)}] + c_4 \times [\gamma\text{-globulin (g/l)}] - c_5 \times [\text{Age (years)}] + c_6 \times \text{Log} [\text{ALT (IU/l)}] - c_7 \times [\text{ApoA1 (g/l)}] - c_8 \times [\text{Sex (female=0, male=1)}] - c_9$, with

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- c_1 comprised between 3.45 and 3.65,
- c_2 comprised between 0.3 and 0.4,
- c_3 comprised between 0.8 and 1,
- c_4 comprised between 0.075 and 0.09,
- c_5 comprised between 0.0015 and 0.003,
- c_6 comprised between 2.1 and 2.5,
- c_7 comprised between 1.55 and 1.75,
- c_8 comprised between 0.35 and 0.45, and
- c_9 comprised between 4 and 4.6.

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- $f4 = d_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - d_2 \times [\alpha 2\text{-globulin (g/l)}] + d_3 \times \text{Log} [\text{GGT (IU/l)}] + d_4 \times [\gamma\text{-globulin (g/l)}] + d_5 \times [\text{Age (years)}] + d_6 \times \text{Log} [\text{Bilirubin (umol/l)}] - d_7 \times [\text{ApoA1 (g/l)}] + d_8 \times [\text{Sex (female=0, male=1)}] + d_9 \times \text{Log} [\text{ALT (IU/l)}] - d_{10}$, with

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- d_1 comprised between 5.3 and 6.7,
- d_2 comprised between 0.45 and 0.5,
- d_3 comprised between 0.8 and 1.2,
- d_4 comprised between 0.06 and 0.08,
- d_5 comprised between 0.0015 and 0.0025,
- d_6 comprised between 1 and 1.2,
- d_7 comprised between 1 and 1.2,
- d_8 comprised between 0.09 and 1.1,
- d_9 comprised between 1.2 and 1.5, and

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- d_{10} comprised between 4 and 5.

- $f5 = z_1 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - z_2 \times \text{Log} [\text{Haptoglobin (g/l)}] + z_3 \times \text{Log} [\text{GGT (IU/l)}] + z_4 \times [\text{Age (in years)}] + z_5 \times \text{Log} [\text{Bilirubin (umol/l)}] - z_6 \times [\text{ApoA1 (g/l)}] + z_7 \times \text{Sex (female=0, male=1)} - z_8$, with

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- z_1 comprised between 4 and 5,

- z_2 comprised between 1.2 and 1.5,

- z_3 comprised between 0.9 and 1.1,

- z_4 comprised between 0.0026 and 0.03,

- z_5 comprised between 1.6 and 1.9,

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- z_6 comprised between 1 and 1.3,

- z_7 comprised between 0.25 and 0.35, and

- z_8 comprised between 5 and 6.

10. The method of claim 9, wherein the logistic function is chosen in the group consisting of:

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- $f1\text{-a} = 6.826 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - 0.479 \times [\alpha 2\text{-globulin (g/l)}] + 1.252 \times \text{Log} [\text{GGT (IU/l)}] + 0.0707 \times [\gamma\text{-globulin (g/l)}] + 0.0273 \times [\text{Age (years)}] + 1.628 \times \text{Log} [\text{Bilirubin (umol/l)}] - 0.925 \times [\text{ApoA1 (g/l)}] + 0.344 \times [\text{Sex (female=0, male=1)}] - 4.544$;

- $f1\text{-b} = 6.552 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - 0.458 \times [\alpha 2\text{-globulin (g/l)}] + 1.113 \times \text{Log} [\text{GGT (IU/l)}] + 0.0740 \times [\gamma\text{-globulin (g/l)}] + 0.0295 \times [\text{Age (years)}] + 1.473 \times \text{Log} [\text{Bilirubin (umol/l)}] - 0.979 \times [\text{ApoA1 (g/l)}] + 0.414 \times [\text{Sex (female=0, male=1)}] - 4.305$

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- $f2 = 10.088 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - 0.735 \times [\alpha 2\text{-globulin (g/l)}] + 2.189 \times \text{Log} [\text{GGT (IU/l)}] + 0.137 \times [\gamma\text{-globulin (g/l)}] + 0.0546 \times [\text{Age (years)}] + 4.301 \times \text{Log} [\text{Bilirubin (umol/l)}] - 2.284 \times [\text{ApoA1 (g/l)}] + 0.294 \times [\text{Sex (female=0, male=1)}] + 0.0312 [\text{Albumin (g/l)}] + 2.109 [\alpha 1\text{-globulin (g/l)}] - 0.136 [\beta 2\text{-globulin (g/l)}] - 0.813 \times \text{Log} [\text{ALT (IU/l)}] - 13.165$.

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- $f3 = 3.513 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - 0.354 \times [\beta 2\text{-globulin (g/l)}] + 0.889 \times \text{Log} [\text{GGT (IU/l)}] + 0.0827 \times [\gamma\text{-globulin (g/l)}] - 0.0022 \times [\text{Age (years)}] + 2.295 \times \text{Log} [\text{ALT (IU/l)}] - 1.670 \times [\text{ApoA1 (g/l)}] - 0.415 \times [\text{Sex (female=0, male=1)}] - 4.311$.

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- $f4 = 5.981 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - 0.481 \times [\alpha 2\text{-globulin (g/l)}]$
 $+ 0.965 \times \text{Log} [\text{GGT (IU/l)}] + 0.0679 \times [\gamma\text{-globulin (g/l)}] + 0.0190 \times$
 $[\text{Age (years)}] + 1.143 \times \text{Log} [\text{Bilirubin (umol/l)}] - 1.097 \times [\text{ApoA1 (g/l)}]$
 $+ 0.092 \times [\text{Sex (female=0, male=1)}] + 1.355 \text{Log} [\text{ALT (IU/l)}] - 4.498.$
- 5 - $f5 = 4.467 \times \text{Log} [\alpha 2\text{-macroglobulin (g/l)}] - 1.357 \times \text{Log} [\text{Haptoglobin}$
 $(\text{g/l})] + 1.017 \times \text{Log} [\text{GGT (IU/l)}] + 0.0281 \times [\text{Age (in years)}] + 1.737 \times$
 $\text{Log} [\text{Bilirubin (umol/l)}] - 1.184 \times [\text{ApoA1 (g/l)}] + 0.301 \times \text{Sex}$
 $(\text{female=0, male=1}) - 5.540.$
- 11. The method of claim 2, wherein the end value of the logistic function is used for
- 10 the diagnosis of cirrhosis.
- 12. The method of claim 1, wherein the end value of the logistic function is used to
- predict the evolution of the disease.
- 13. The method of claim 1, wherein the end value of the logistic function is used for
- the choice of a suitable treatment for the patient.
- 15 14. The method of claim 1, wherein the end value of the logistic function is used in
- the decision of performing a liver biopsy on said patient.
- 15. The method of claim 2, wherein said patient suffers from a disease involving
- liver fibrosis, optionally developing to cirrhosis.
- 16. The method of claim 15, wherein said disease is included in the group
- 20 consisting of hepatitis B and C, alcoholism, hemochromatosis, metabolic
- disease, diabetes, obesity, autoimmune liver disease, primary biliary cirrhosis,
- $\alpha 1$ -antitrypsin deficit, Wilson disease.
- 17. The method of claim 15, wherein said disease is hepatitis C virus infection.
- 18. Kit of diagnosis of an inflammatory, a fibrotic or a cancerous disease in a
- 25 patient, comprising instructions allowing to determine the presence of said
- inflammatory, fibrotic or cancerous disease in said patient, after the dosage of
- biochemical markers.
- 19. Kit of diagnosis of liver fibrosis and/or liver necroinflammatory lesions in a
- patient, comprising instructions allowing to determine the presence of liver
- 30 fibrosis and/or liver necroinflammatory lesions in said patient, after the dosage
- of biochemical markers.